The relationship of corneal topographic parameters with corneal and lens densitometers in patients with keratoconus

Corneal and lens densitometers in keratoconus

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Abstract

Aim: The aim of this study was to investigate the relationship between corneal-lens densitometry and the corneal topographic parameters in keratoconus patients.

Material and Methods: The database of the Pentacam® HR device between 2017 and 2019 was analyzed retrospectively. A total of 85 eyes of 85 keratoconus patients and 55 right eyes of 55 healthy control subjects were included in the study. The corneal density was measured manually in the full-thickness cornea with a diameter of 2 mm in the corneal apex. The lens density was measured manually in the pupillary area with a diameter of 2 mm throughout the whole central lens thickness.

Results: Maximum corneal density was significantly higher in keratoconus patients [15.96 ± 2.52 (10.2-20.0)] compared with healthy control subjects [14.22 ± 2.41 (9.0-19.3)] (p<0.001). The mean lens density [7.55 ± 0.56 (7.0-9.1)] was lower in keratoconus patients compared with healthy control subjects [7.93 ± 1.07 (7.0-11.3); p=0.007)]. Additionally, the mean keratometry value and the maximum lens density value were negatively correlated with each other (p=0.018).

Discussion: Corneal density is increased and the lens density decreased in keratoconus patients. It was determined that the lens density decreased while the corneal density increased in keratoconus patients. These results suggest that several factors may cause corneal and lenticular alterations in these patients.

Keywords

Cornea; Corneal topography; Keratoconus; Lens

Introduction

Keratoconus is an ectatic disease leading to thinning of the cornea, irregular astigmatism, and severe visual loss. This progressive pathology is the most common cause of corneal transplantation in developing countries [1].

Keratoconus is considered an important health problem since it starts at early age and exposes the person to visual loss in the critical period of education and development [2]. Its symptoms begin to appear during puberty and early adulthood and tends to progress until the 4th decade [1]. Although there is no consensus about the prevalence of the disease, a rate between 1/500 and 1/2000 is estimated [3].

The etiology of the keratoconus is not clear and continuous eye scratching is reported as a risk factor [4]. It can be associated with other ocular and systemic pathologies such as vernal keratoconjunctivitis, Down syndrome, retinitis pigmentosa, Turner's syndrome, and Ehlers-Danlos syndrome.

The diagnosis of keratoconus is facilitated by topographic maps of the cornea in addition to the clinical examination. The Scheimpflug tomography imaging device is currently being used as a diagnostic, non-invasive imaging method that provides objective information about corneal topographic measures in these patients. In addition, it assesses corneal and lenticular density (transparency) [5-7].

Corneal densitometry is reported to be increased in subclinical keratoconus and related to the stage of keratoconus [5-8]. It is also used to monitor the progression of the disease and the efficacy of some treatment modalities [9]. In the literature, there is no study evaluating lenticular changes in patients with established keratoconus diagnosis. In this study, we aimed to investigate corneal and lenticular densitometry changes taking place in keratoconus patients.

Material and Methods

The study was performed by retrospective analyses of the archive data (between January 2017 and January 2019) of Pentacam® HR Scheimpflug rotating camera system (Oculus Inc., Wetzlar, Germany). It was granted by the Clinical Research Ethics Committee of the Kahramanmaras Sutcu Imam University Faculty of Medicine (protocol number: 365, decision number-date: 14/2019).

Individuals between 18-35 years old were taken into the study and divided into two groups as keratoconus group (KG) and a healthy control group (CG).

The following criteria were used for the diagnosis of keratoconus:

• a keratometry (K) value of more than 47.2 diopters (D);

• an inferior-superior asymmetry for the mean K value of more than 1.4 D;

• a keratoconus percentage index of more than 60%.

The anterior and posterior elevations of the cornea were evaluated according to the best fit sphere (BFS) reference in suspicious cases. The differences were considered abnormal if they were above 7 μm for the anterior and 16 μm for the posterior elevations [5].

The control group consisted of healthy individuals with no systemic disease between 18-35 years of age with low refractive error (spherical<± 3 D, cylindrical ± 1.5 D), who did not undergo any surgical interventions.

Patients with corneal pathology other than keratoconus (keratitis, peripheral corneal degenerations, nephelion, etc.), high refractive error (spherical >± 3 D, cylindrical >± 1.5 D), previous refractive surgery, corneal transplantation, any surgical treatments for keratoconus, a history of cataract surgery, uveitis, ocular trauma and systemic diseases and with images of poor quality were excluded from the study. In addition, patients with K-max values of >58.0 D were excluded from the study since a steep cornea can alter corneal densitometry values.

Horizontal (K1) and vertical (K2) keratometry values, mean keratometry (K-mean), maximum keratometry (K-max), central corneal thickness (CCT) and thinnest corneal thickness (TCT), corneal volume (C-vol), anterior corneal elevation (ACE), posterior corneal elevation (PCE) from all individuals were obtained. Corneal densitometry (CD) and lens densitometry (LD) were measured by relevant measurement modules of the Pentacam HR device in addition to the data which have been provided automatically. CD was measured manually in the full-thickness cornea with a diameter of 2 mm in the corneal apex, and the mean corneal density (CD-mean) and maximum corneal density (CD-max) values were calculated (Figure 1). Lens density was measured manually in the pupillary area with a diameter of 2mm throughout the whole central lens thickness in the 3D mode of the device. The mean lens density (LD-mean) and maximum lens density (LD-max) values were obtained (Figure 2). The densities, an index of backscattered light from the tissue analyzed, are given as numerical values between 0 (completely transparent) and 100 (completely opaque). The images of 90-270° were assessed for standardization.

Statistical analysis

The statistical analysis of the data was performed using SPSS 20.0 software (SPSS Inc., Chicago Ill, USA). The normality of the data was tested by the Kolmogorov-Smirnov and the Shapiro-Wilk tests. In normally distributed variables, the difference between the groups in terms of quantitative variables was evaluated by the Independent samples t-test. The correlations between the variables were analyzed with the Pearson's correlation test and if the p-value <0.05, r (correlation coefficient) was assessed. The Chi-Square test was used to determine the frequency distributions between the categorical data. The level of significance was set at $p<0.05$.

Results

A total of 85 eyes of 85 patients in the keratoconus group and 55 eyes of 55 healthy individuals in the control group were investigated in the study. The eye with the worst keratometric value in KG and the right eyes in CG were selected for analyses. The mean age of the patients was 26.25 ± 4.89 (18-35) years in KG and 25.87 ± 4.99 (19-35) years in CG (p=0.662). The genders were also similar between KG (female/male: 46/39) and CG (female/male: 35/20) (p=0.265).

The corneal and lenticular measurements are demonstrated in (Table 1). As expected, corneal keratometry values in KG were higher than in CG. The keratoconus group had a mean keratometry value of 46.88 ± 2.29 (42.9-53.0), which was higher compared to the control group (43.21 ± 1.39 (40.0-46.0), p<0.001). While the K-max ranged between 43.0 D and 58.0 D,

Table 1. Comparison of topographic and densitometric parameters between keratoconus and control groups

	Group KC (n=85)	Group CG (n=55)	p
K1 (D)	45.24 ± 2.30 (40.6-52.0)	42.65 ± 1.42 (39.0-46.0)	<0.001
K2 (D)	48,67 ± 2,48 (44.3-54.4)	43.76 ±1.41 (40.0-46.0)	<0.001
K-mean (D)	46.88 ± 2.29 (42.9-53.0)	43.21 ± 1.39 (40.0-46.0)	<0.001
K-max (D)	52.71 ± 3.26 (43.0-58.0)	44,22 ± 1.48 (40.0-47.0)	<0.001
CCT (μm)	470.52 ± 29.06 (377-567)	545.73 ± 18.86 (500-583)	<0.001
TCT (μm)	460,02 ± 29.15 (357-550)	540.62 ± 17.43 (510-579)	<0.001
C-vol (mm3)	56.70 ± 2.79 (50.2-68.6)	60.37 ± 2.54 (52.0-66.2)	<0.001
ACE (μm)	21.39 ± 6.65 (20-35)	3.25 ± 1.38 (1-6)	<0.001
PCE(μm)	42.44 ± 8.81 (19-60)	6.58 ± 2.16 (3-12)	<0.001
CDAN-mean	11.57 ± 1.58 (8.2-16.5)	11.28 ± 1.88 (8.0-16.0)	0.325
CDAN-max	15.96 ± 2.52 (10.2-20.0)	14.22 ± 2.41 (9.0-19.3)	<0.001
LD-mean	7.55 ± 0.56 (7.0-9.1)	7.93 ± 1.07 (7.0-11.3)	0.007
LD-max	10.65 ± 3.78 (7.1-25.1)	11.35 ± 3.68 (8.0-24.3)	0.282

Independent samples t test; α=0.05
Data are expressed as a mean value ± SD (standard deviation) (min-max); p<0.05 is statistically significant; Group KG: patients with keratoconus, Group CG: healthy control group. K1: horizontal keratometry value, K2: vertical keratometry value, K-mean: mean keratometry value, K-max: maximum keratometry value, CCT: central corneal thickness, TCT: thinnest corneal thickness, C-vol: corneal volume, ACE: anterior corneal elevation, PCE: posterior corneal elevation, CDAN-mean: mean corneal densitometry value, CDAN-max: maximum corneal densitometry value, LD-mean: mean lens densitometry value, LD-max: maximum lens densitometry value

Figure 1. The corneal density measurement with Pentacam® HR Scheimpflug rotating camera system

Table 2. Correlation results of topographic and densitometric measurements between keratoconus and control groups

Correlations	Group KC (n=85)	Group CG (n=55)
K-mean - LD-mean	r=-0.107, p=0.330	r=0.032, p=0.819
K-max - LD-mean	r=-0.700, p=0.525	r=0.042, p=0.761
CCT - LD-mean	r=0.013, p=0.908	r=0.036, p=0.794
TCT - LD-mean	r=-0.027, p=0.806	r=0.039, p=0.776
C-vol - LD-mean	r=-0.093, p=0.396	r=0.032, p=0.818
ACE - LD-mean	r=0.094, p=0.391	r=0.147, p=0.285
PCE - LD-mean	r=0.100, p=0.363	r=-0.051, p=0.711
CDAN-mean - LD-mean	r=0.207, p=0.058	r=0.390, p=0.003
CDAN-max - LD-mean	r=0.103, p=0.349	r=0.200, p=0.144
K-mean - LD-max	r=-0. 256, p=0.018	r=-0.061, p=0.658
K-max - LD-max	r=-0.151, p=0.168	r=-0.051, p=0.712
CCT - LD-max	r=0.155, p=0.157	r=-0.164, p=0.232
TCT - LD-max	r=0.086, p=0.435	r=-0.142, p=0.302
C-vol - LD-max	r=-0.016,p=0.883	r=-0.178, p=0.194
ACE - LD-max	r=-0.067, p=0.544	r=0.106, p=0.443
PCE - LD-max	r=-0.005, p=0.966	r=0.014, p=0.918
CDAN-mean - LD-max	r=0.001, p=0.995	r=0.211, p=0.122
CDAN-max - LD-max	r=-0.030, p=0.783	r=0.167, p=0.223

Pearson correlation analysis; r=correlation coefficient, p<0.05 is statistically significant; Group KG: patients with keratoconus, Group CG: healthy control group
K-mean: mean keratometry value, K-max: maximum keratometry value, CCT: central corneal thickness, TCT: thinnest corneal thickness, C-vol: corneal volume, ACE: anterior corneal elevation, PCE: posterior corneal elevation, CDAN-mean: mean corneal densitometry value, CDAN-max: maximum corneal densitometry value, LD-mean: mean lens densitometry value, LD-max: maximum lens densitometry value
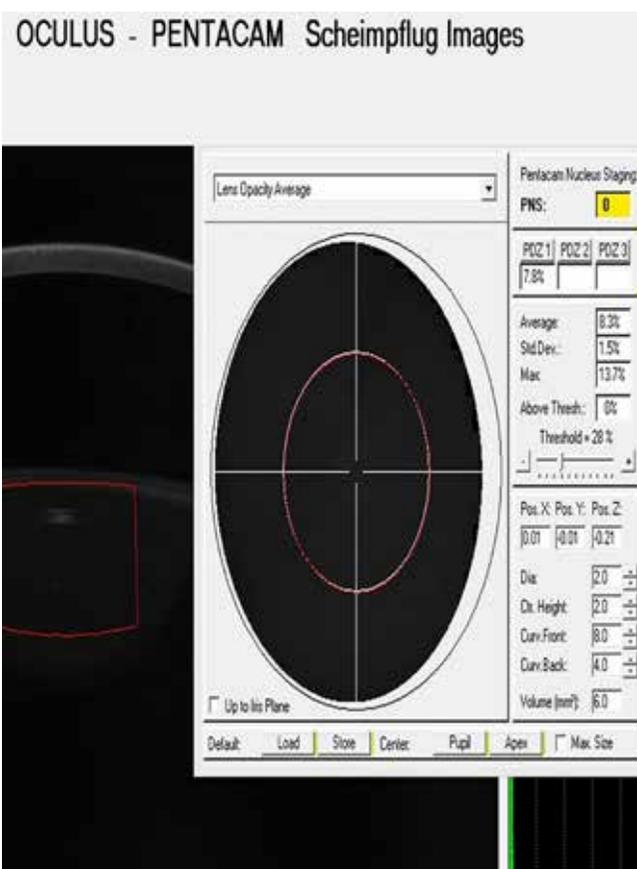

Figure 2. The lens density measurement with Pentacam® HR Scheimpflug rotating camera system

K-max in the control group ranged between 40.0 and 47.0D. CD-max was significantly higher in KG [15.96 ± 2.52 (10.2-20.0)] compared to that in CG [14.22 ± 2.41 (9.0-19.3)] (p<0.001). LD-mean was 7.55 ± 0.56 (7.0-9.1) in KG, which is lower than LD-mean in CG [7.93 ± 1.07 (7.00-11.3)] (p=0.007). While K-mean and LD-max in the keratoconus group were negatively correlated (r=-0.256, p=0.018), such a correlation was not confirmed in the control group (p=0,658). Correlation results of the topographic and densitometric measurements between keratoconus and control groups were listed in Table 2.

Discussion

Keratoconus is a disease of unknown etiology that causes thinning of the corneal layers, especially the corneal stroma [10]. However, it remains unclear whether there is a change in the lens structure in patients with keratoconus. This study is the first study in the literature in which corneal and lens densitometry were evaluated by objective and quantitative methods in this patient group.

In this study, we found that cornea had higher density while the lens showed lower density in keratoconus patients. Although the former finding is expected in keratoconus patients, the decreased lens density may need further explanation.

The tissue density in the Pentacam device reflects the amount of backscattered light on a predetermined tissue area and it work swith the help of certain add-on software on the Standard software. There is no established explanation for decreased lenticular density in KG since our study is the first on this issue. But, some theoretical comments may be brought forward to elucidate the mechanism. One of the explanations may arise from the biochemical characteristics of aqueous humor in keratoconus patients. The limited information suggests that keratoconus patients may have a protective-antioxidative microenvironment in their aqueous humor [11-13] and it is known that penetrating graft survival outcomes are excellent in keratoconus patients [14]. Based on these data, it can be speculated that the aqueous humor of keratoconus patients may have some protection for the lens. The negative correlation of mean keratometry value with maximum lens density in keratoconus patients, but not in control patients, might also support our hypothesis. Additionally, this may imply that as the keratoconus progresses, lenticular protection increases.

It might be speculated that the same pathological-physiological event may lead to corneal thinning on one side, and, on the other side, it creates some kind of lenticular protection [4, 11]. Despite the fact that an argument not depending directly on evidence- based medicine may not seem analytical, such speculations may have some scientific merit as well [15]. Our hypothesis, other alternative mechanisms, and the clinical implications of decreased lens density in these patients deserve to be investigated with further researches.

There are several researches in the literature regarding the corneal density in keratoconus. It was stated that the increased corneal density in subclinical keratoconus patients might be a guide for the diagnosis of keratoconus [5]. In another similar study, Lopes et al. [8] found an increase in corneal densitometry in the central region of keratoconus patients. Similar to these studies, the maximum corneal densitometry measurements were found to be higher than the control group in our study. This finding may indicate a loss of focal transparency in the apical region since our measurements were taken from the corneal apex.

The retrospective character of the study and the fact that lens densitometry measurements were made only from the central 2 mm part of the cornea and lens are the limitations of the study. Density measurements in the whole diameter of the lens can be determined by future studies. Another limitation of the study might be that elderly patients were excluded from the study. But we chose younger age in our study due to the decrease in keratoconus progression by age and the expected increase in lens density with older age.

In conclusion, decreased lenticular density was found while had elevated corneal density in keratoconus patients in our study. These results suggest that several factors that simultaneously affected the cornea and lens which thought to have anti-inflammatory effects, such as aqueous humor proteins, may play a role. Future studies to be conducted at the molecular level with developing technology will open up new horizons by providing a clearer understanding of the pathophysiological mechanisms related to this disease.

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